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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,134	10/20/2002	Chandrasekhar Satishchandran	AM100013	5538

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,134	SATISHCHANDRAN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-173* is/are pending in the application.

4a) Of the above claim(s) *68-106 and 169* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *107-168 and 170-173* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04, 3/02/04*. 5/17/04, 3/04/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the Restriction requirement in the reply filed on 10/20/2005 is acknowledged. The traversal is on the ground(s) that a search of RNA interference would encompass any references useful in the examination of methods and nucleic acid compositions useful in RNA interference. This is not found persuasive because a search for an isolated nucleic acid molecule would not necessarily reveal art on a method of inducing RNAi of a target gene and further would not necessarily reveal art on a multitarget partially double stranded RNA molecule and further would not necessarily reveal art on a method of making a composition comprising two or more different double stranded RNA molecule. As stated in the previous Office action filed on 09/20/2005, the subject matter is divergent and non-coextensive and it is therefore a burden to search these inventions in a single application.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Application

Claims 68-173 are pending. Claims 107-168 and 170-173 are currently under examination. Claims 68-106 and 169 are withdrawn as being drawn to a non-elected invention.

Priority

The priority date granted for claims 107-136 and 150-155 is 06/25/2005. The priority date granted for claims 137-168 and 170-173 is 04/19/2000. Applicant does not receive the

benefit of the earlier applications 60/130,377 and PCT/US00/10555 because the prior applications do not provide adequate support for the claims of the instant application.

Claims 107-136 and 150-155 are drawn to a multitarget partially double stranded RNA comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene and further drawn to an expression vector comprising two or more promoters capable of expressing two or more double stranded RNA. The prior applications 60/130,377 and PCT/US00/10555 disclose a partially double stranded polynucleotide targeted to a single gene or more than one gene and further disclose an expression vector capable of expressing two or more double stranded RNA molecules. The prior applications 60/130,377 and PCT/US00/10555 do not disclose a multitarget partially double stranded RNA molecule comprising two or more "different" double stranded sequences and further do not disclose an expression vector comprising two or more promoters capable of expressing two or more double stranded RNA.

Claims 137-168 and 170-173 are drawn to an expression vector wherein the vector encodes two or more different double stranded RNA molecules that are complementary to two or more target sequences. The Provisional application 60/130,377 discloses an expression vector encoding a single double stranded RNA molecule or a single stranded sense and antisense RNA molecule that can form a double stranded RNA molecule. The Provisional application 60/130,377 does not contemplate an expression vector wherein the vector encodes two or more different double stranded RNA molecules.

If Applicant believes the prior application provides support then applicant must point, with particularity, to where such support can be found in the specification of the prior application.

Therefore, the priority date granted to claims 107-136 and 150-155 is 06/25/2005 and the priority date granted to claims 137-168 and 170-173 is 04/19/2000.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 107-136 and 150-155 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 107-136 are drawn to a multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene. Claims 150-155 are drawn to an expression vector wherein said two or more different double stranded RNA sequences are expressed using two or more promoters.

The specification, on page 8, discloses a polynucleotide comprising an RNA that is targeted to one or more genes. The specification further recites on page 8 " a partially double

stranded RNA polynucleotide..." The specification on page 20 discloses an expression vector capable of generating two or more double stranded RNA. The specification does not contemplate a multitarget partially double stranded RNA molecule comprising "two or more *different* double stranded RNA sequences". Further, the specification does not contemplate an expression vector wherein the vector comprises two or more promoters capable of expressing two or more double stranded RNA. If Applicant believes that such support is present in the specification and claimed priority documents, Applicant should point, with particularity, to where such support is to be found.

Therefore, the effective filing date of claim 107-136 and 150-155 are considered, for purposes of prior art to be 06/24/2005, which is the filing date of the amended claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 107-108, 113-119, 121, 123, 125, 127-138, 141-148, 156-159, 163, 165, 167, 168 and 170-172 are rejected under 35 U.S.C. 102(b) as being anticipated by Taira et al. (U.S. Patent No. 5,500,357).

The instant claims are drawn to a multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene or an expression vector encoding a multitarget partially double-stranded RNA molecule, one or more of said different double-stranded RNA sequences comprises a sense polynucleotide and an antisense polynucleotide that form a hairpin, the double-stranded RNA sequences are separated by cleavage sequences, the cleavage sequences are autocatalytic sequences or splice sites and further wherein at least one target gene is from a single target pathogen, the target genes are from more than one target pathogen, said target pathogen is a virus, said target gene is associated with a disease or disorder in a mammal, said two or more sequences of said target gene are selected from the group consisting of regions as listed and further drawn to a composition comprising the multitarget partially double-stranded RNA, the double stranded RNA is encoded by a DNA molecule, the multitarget partially double-stranded RNA is expressed using a promoter as listed and the expression vector is a plasmid, phage or recombinant virus.

Taira et al. teach a multitarget partially double stranded RNA molecule comprising from two or more different double stranded RNA sequences that are substantially homologous and complementary to 2 or more sequences of a target gene (see Figure 3). Taira et al. further teach said multitarget partially double stranded RNA molecule comprises a sense polynucleotide and an antisense polynucleotide separated by a non-base paired sequence and the sense and antisense polynucleotide form a hairpin (see Figure 9), two or more different double stranded RNA sequences are separated by cleavage sequences, the cleavage sequences are autocatalytic cleavage sites and the multitarget partially double stranded RNA lacks a polyadenylation signal

(see Figures 7A). Taira et al. further teach the multitarget partially double stranded RNA molecule can target one gene or more than one gene (see column 7, lines 23-29). Taira et al. teach a DNA molecule encoding the multitarget partially double stranded RNA molecule or two or more double stranded RNA molecules and further teach a plasmid expression vector wherein the partially double stranded RNA molecule is expressed using a T7 bacteriophage promoter (see Figure 3). Taira et al. further teach an expression vector for reducing or inhibiting the function of the target gene wherein the expression vector encodes two or more double stranded RNA sequences complementary to two or more target sequences in one target gene (see Figure 13).

Claims 107, 109, 111-117, 119, 121, 123-137, 139, 141-143, 144-148, 156-157, 159, 163, 165, 167, 168 and 170-173 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Nucleic Acids Research 1992).

The instant claims are drawn to a multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene or an expression vector encoding a multitarget partially double-stranded RNA molecule, at least 11 to 30 nucleotides are involved in each different double stranded sequences, each different double-stranded RNA sequence comprises at least one segment of 30 contiguous nucleotides with a homology of at least 50% to a similar 30 nucleotide region of the target sequence, wherein said multitarget partially double-stranded RNA is between about 100 and 10,000 polynucleotides in length, the double-stranded RNA sequences are separated by cleavage sequences, the cleavage sequences are autocatalytic sequences or splice sites and further wherein at least one target gene

is from a single target pathogen, said target pathogen is a virus, said target gene is associated with a disease or disorder in a mammal, said two or more sequences of said target gene are selected from the group consisting of regions as listed and further drawn to a composition comprising the multitarget partially double-stranded RNA wherein the composition further comprises an agent that facilitates polynucleotide uptake by a cell, the double stranded RNA is encoded by a DNA molecule, the multitarget partially double-stranded RNA is expressed using a promoter as listed and the expression vector is a plasmid, phage or recombinant virus.

Chen et al. teach a multitarget partially double stranded RNA molecule comprising from 2 to 9 different double stranded RNA sequences that are substantially homologous and complementary to 2 or more sequences of an HIV target gene (see Figure 2). Chen et al. teach said multitarget partially double stranded RNA is 400 polynucleotides in length and further wherein each partially double-stranded RNA molecule is at least 30 nucleotides in length and further wherein the multitarget partially double stranded RNA molecule comprises a segment of at least 30 nucleotides wherein at least 15 nucleotides are homologous (see Figure 2). Chen et al. teach two or more different double stranded RNA sequences are separated by cleavage sequences, the cleavage sequences are autocatalytic cleavage sites, the target gene is from a single HIV env transcribed gene and the multitarget partially double stranded RNA lacks a polyadenylation signal (see Figures 1 and 2). Chen et al. further teach a composition comprising said multitarget partially double stranded RNA molecule comprising an agent which facilitates uptake in the cell (see page 4582 column 1). Chen et al. teach a DNA molecule encoding the multitarget partially double stranded RNA molecule and a plasmid expression vector wherein the partially double stranded RNA molecule is expressed using a T7 bacteriophage promoter (see

Figure 1). Chen et al. further teach an expression vector for reducing or inhibiting the function of the target gene wherein the expression vector encodes two or more double stranded RNA sequences complementary to two or more target sequences in one target gene (see page 4586 column 2 and Figure 6).

Claims 150-155 are rejected under 35 U.S.C. 102(e) as being anticipated by Taira et al. (US 2005/0197315).

The instant claims are drawn to an expression vector encoding two or more double stranded RNA wherein the vector comprises two or more promoters and further wherein the promoters are RNA pol III promoters.

Taira et al. teach an expression vector comprising two pol III promoters capable of generating multiple double stranded RNA molecules (see Figures 2, 18 and 25)

Thus, Taira et al. anticipates claims 150-155 of the instant application.

Claims 107,117, 119-120, 137, 157, 159-160, 164 and 166 are rejected under 35 U.S.C. 102(e) as being anticipated by Ruiz et al. (U.S. Patent No. 5,912,149).

The instant claims are drawn to a multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of a target gene wherein the target gene is HBV.

Ruiz et al. teach a multitarget partially double-stranded RNA molecule comprising two different double stranded RNA sequences that are complementary to two sequences of a HBV

target gene (see Figure 1A and 1B). Ruiz et al. further teach the multitarget partially double-stranded RNA molecules can be used to target other pathogens and cancer associated genes such as human T-cell leukemia virus (see column 3, lines 14-22). Ruiz et al. further teach an expression vector which encodes two different double stranded RNA sequences that are complementary to a HBV target gene (see column 8, lines 30-44).

Thus, Ruiz et al. anticipates claims 107,117, 119-120, 137, 157, 159-160, 164 and 166 of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Kimberly Chong
Examiner
Art Unit 1635